Application No. 10/049,975
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## REMARKS

Pending claims 1-6, 27-37, 45-47, 52, 54, and 56-62 have been rejected under 35 U.S.C. § 112 for indefiniteness and lack of enablement. These rejections are respectfully traversed in light of the claim amendments and the remarks given below. Claim 1 has been amended to more explicitly specify that which Applicants regard as the invention. The amendments are supported by the specification and drawings, and no new matter has been added. Reconsideration is requested.

### The Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 27-37, 45-47, 52, 54, and 56-62 are rejected as allegedly lacking enablement. Claim 1 is allegedly not enabled for reasons specified in the Office Action mailed March 8, 2006, which states that the claim fails to recite any means for preventing the dye from contacting or being near the fluorophor in the complex at the surface. The rejection is respectfully traversed.

In the method of claim 1, a dye is used to improve the signal-to-noise ratio (S/N) of the fluorescence signal used as a measure of the substance being assayed. The dye accomplishes this by eliminating more of the "volume fluorescence" (i.e., fluorescence in the bulk solution which is due to the portion of the compound containing the fluorophor that does not bind to the surface) than of the "surface" fluorescence (i.e., fluorescence referable to the bound complex). No means of preventing the dye from contacting or approaching the fluorophor in the surface-bound complex is required in order to practice the claimed method, because the dye reduces the volume fluorescence more than it



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reduces the surface fluorescence. This is simply the result of the dye being distributed throughout the solution, with the effect that only the small proportion of the dye present near the surface is able to affect surface fluorescence (excited by evanescent light), whereas most of the dye is able to affect volume fluorescence (excited by scattered light entering the solution). This effect is demonstrated in Figure 6a, where it is apparent that as dye concentration is increased, the volume fluorescence (diamonds) declines to a much greater extent than the surface fluorescence (squares). Thus, the dye has a relative effect on surface fluorescence, not an absolute effect as asserted in the rejection.

The Office Action mailed August 28, 2006 states that "the claims do not set forth how detection of the fluorophor is possible when a dye is present that quenches the fluorophor." Office Action at p. 2, fourth paragraph. It should be apparent from the above discussion that the dye does not "quench" the fluorophor bound at the surface; as illustrated in Fig. 6a, the dye selectively reduces background noise (volume fluorescence) more than it reduces the signal (surface fluorescence) used to measure the substance being assayed. This effect is consistent over the full range of dye concentrations tested in Fig. 6.

Therefore, Applicants believe that the claims are enabled and respectfully request withdrawal of this rejection.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-6, 27-37, 45-47, 52, 54, and 56-62 are rejected as allegedly being indefinite because claim 1 is allegedly vague in several aspects. The rejection is respectfully traversed.



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Claim 1 allegedly fails to recite the relationship among R1, the substance being assayed, and the compound containing the fluorophor. While Applicants believe that the relationship was previously clear in the claim as read in light of the specification, the relationship is more explicitly specified in amended claim 1, which recites "wherein said complex is formed by covalent or non-covalent interactions of reaction partner R1 with the substance being assayed and by covalent or non-covalent interactions of the compound containing at least one fluorophor with the substance being assayed". Thus, the claim specifies that the substance being assayed binds to each of R1 and the compound containing at least one fluorophor, through covalent or non-covalent interactions. Overall, the claim states that R1 is bonded to the surface, that R1 is bound to the substance being assayed, and that the substance being assayed is bound to the compound containing at least one fluorophor. In this way, the substance being assayed is bound to the surface, and its presence is signaled by fluorescence derived from excitation of the fluorophor by evanescent light. The relationship among the components of the surface-bound complex is clearly stated by claim 1.

Claim 1 is allegedly unclear regarding the function of the dye in assaying the substance, and how the dye is kept away from the fluorophor bound to R1 on the surface. As discussed for the enablement rejection above, the dye is not kept away from the fluorophor bound to R1 on the surface. The function of the dye, which is evident from claim 1 as read in light of the specification, is to increase the S/N of the fluorescence signal used to measure the substance being assayed. In order to further



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specify the use of the dye in the claimed method, claim 1 has been amended to recite "wherein said dye is present in the solution at a concentration sufficient to absorb 70% or more of the light entering the solution within 1 mm above the top of said surface". The specification at page 9, lines 4-5 states: "The concentration of dye can be adjusted, depending on the dye, so that the penetrating light can basically be absorbed within 1 mm above the surface." Later in the same paragraph (at p. 9, lines 11-12) the term "basically absorbed" is explained as "an intensity cancellation of 70%, preferably 80% and especially preferred at least 90%." The amended claim explicitly provides a benchmark for using the dye in a manner which improves the S/N of the surface fluorescence signal, although Applicants believe this use of the dye was clear as well without this amendment, from a reading of the specification.

Claim 1 allegedly lacks a correlation step that relates the measured fluorescence to the presence of the substance being assayed. Although such a correlation was believed to be already implicit in the claim, the claim has been amended to more clearly state that the step of exciting the fluorophor includes "measuring the fluorescence produced as a measure of the substance being assayed".

Claim 1 is also allegedly unclear because it does not specify what else is contained in the "at least one compound containing a fluorophore". The specification describes the compound containing a fluorophore, for example, at page 5, line 39 through page 6, line 20. From the specification it is clear that the compound can contain a variety of substances in addition to the fluorophor, such as a chemical moiety containing a binding site for the

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substance being assayed, a protein (e.g., antibody or phycobili protein), a small molecular weight compound, or a protective group than can be split off to release a fluorophor. Applicants do not intend to limit this aspect of the claim, and it is believed that the term "at least one compound containing a fluorophore" is clear and definite when read in light of the specification.

For each of the reasons discussed above, Applicants believe that the claims are clear and definite. The withdrawal of the rejection is respectfully requested.

Applicants submit that all claims are in condition for allowance and such action is respectfully requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

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